REMARKS

I. Status of Claims

Claims 1, 2, 4-7, 9-11, 15-26, and 41-61 will be pending, upon entry of this response. Claim 9 has been revised to recite "amorphous calcium phosphate." Applicant also has amended claims 1 and 7 to prescribe that the claimed complex is formed by binding, under alkaline conditions, amorphous calcium (fluoride) phosphate with phosphopeptide. In addition, applicant has revised claims 6 and 50 to qualify the alkaline conditions, relating them to a pH range of above 7.0 to about 9.0. Support of these recitations can be found in the specification, for example, at page 3, lines 7-10, and at page 12, Example 1.

II. Response to Restriction Requirement

Upon entry of claim revisions previously presented, the examiner has required applicant to elect either of Groups IV and V. In response, applicant provisionally elects Group V, with traverse.

The examiner's rationale of the restriction requirement seems to be that the effects of forming the complex under alkaline conditions are negated upon exposure of the formed complex to acidic conditions. With this understanding, the examiner concludes that claim 1 encompasses both alkaline and acidic complexes; hence, he requires applicant to elect either a complex that is characterized as "alkaline" or one that need not be "alkaline."

At the outset, applicant would emphasize that the examiner is mistaken to qualify a complex, as claimed, in terms of a "pH" property. Rather, it is an important distinguishing feature of the claimed complex that it is formed at a pH that is alkaline; that is, alkaline conditions must pertain during the binding of amorphous calcium (fluoride) phosphate with phosphopeptide. To highlight this feature, applicant has revised claims 1 and 7 to define the complex with more specific reference to the formation step.

Just as the form (or phase) of calcium phosphate varies with solution pH, the capacity and efficiency of calcium phosphate in binding phosphopeptide also varies as a function of the pH of the solution where the binding occurs. As the specification describes and the accompanying declaration by Dr. Reynolds attests, the form of calcium phosphate under acidic conditions, $CaHPO_4$, is known for poor phosphopeptide-binding affinity. In sharp contrast, amorphous calcium (fluoride) phosphate has greater capacity and affinity to binding phosphopeptide. It was applicant's discovery that, under alkaline conditions, phosphopeptide effectively captures and stabilizes calcium phosphate in the form of amorphous calcium (fluoride) phosphate, by forming a certain structure in the resulting complex.

Example 2B in the present specification, at pages 15-17, details NMR studies to determine the structure in question, which is elucidated in the Reynolds declaration by reference to appended structural models. As the structural models clearly show, phosphopeptide forms outer layers and thereby completely surrounds amorphous calcium (fluoride) phosphate at the core.

In sections 8-10 of his declaration, Dr. Reynolds attests that, with this structure, the phosphopeptide effectively shields the core from hydrogen cations and hydroxide anions in an aqueous solution of the complex. As a consequence, the inventive complex is resistant to the effects of solution pH, for example, in the range of pH 4.5 to 9, as recited in claims 54 or 55.

In summary, the record shows that: (1) there is no "pH" property of the claimed complex, but instead a pH of complex formation that does distinguish the claimed invention from the prior art; and (2) the claimed complex, once formed under alkaline conditions, has a structure that is stable against pH changes in the surrounding environment. Accordingly, no reasonable basis exists for the examiner's unsupported contention that the effects of forming a

complex under alkaline conditions, as recited, somehow may be negated upon exposure of the complex to acidic conditions.

Thus, the present claims cannot divided between categories that are defined on the basis of some post-formation, pH-mediated change, let alone a non-existent "pH" property. For this reason, applicant respectfully requests withdrawal of the restriction requirement and examination of claims of both Groups IV and V together in this application.

Applicant believes that the present application otherwise is in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 24 December 2002 By S. A. Bent

FOLEY & LARDNER
Washington Harbour
3000 K Street, N.W., Suite 500
Washington, D.C. 20007-5143
Telephone: (202) 672-5404
Facsimile: (202) 672-5399

Stephen A. Bent
Attorney for Applicant
Registration No. 29,768

VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Four Times Amended) A stable soluble calcium phosphate complex comprising [phosphopeptide-stabilized] amorphous calcium fluoride phosphate and phosphopeptide that stabilizes said amorphous calcium fluoride phosphate, wherein said phosphopeptide includes the amino acid sequence Ser(*P*)-Ser(*P*)-Ser(*P*)-Glu-Glu (SEQ ID NO: 5) and wherein said complex is formed by binding said amorphous calcium fluoride phosphate with phosphopeptide [is formed] in alkaline conditions.

6. (Three Times Amended) A complex according to claim 1, wherein said alkaline conditions are pH of [about] above 7.0 to about 9.0.

7. (Four Times Amended) A stable soluble calcium phosphate complex comprising [phosphopeptide-stabilized] amorphous calcium phosphate and phosphopeptide that stabilizes said amorphous calcium phosphate wherein said phosphopeptide includes the amino acid sequence Ser*(P)*-Ser*(P)*-Ser*(P)*-Glu-Glu (SEQ ID NO: 5) and wherein said complex is formed by binding said amorphous calcium phosphate with phosphopeptide [is formed] in alkaline conditions.

9. (Three Times Amended) A complex according to claim 7, wherein said amorphous calcium [fluoride] phosphate is of the approximate formula $[Ca_3(PO_4)_{1.87}(HPO_4)_{0.2}(H_2O)_x]$, wherein $x \geq 1$.

50. (Amended) The complex according to claim 7, wherein said alkaline conditions are pH of [about] above 7.0 to about 9.0.